REMARKS

Claims 9-20 and 41-55 were pending in this application. Claims 9-20, 44 and 49 have been canceled without prejudice to Applicants' right to prosecute their subject matter in the present application and in related applications. Claims 41, 43, 45, 48, 54 and 55 have been amended without any intent of disclaiming equivalents thereof. Accordingly, claims 41-43, 45-48 and 50-55 are pending and presented for consideration.

Claim amendments

Support for the claim amendments can be found in the specification, including the claims as originally filed. Claims 43, 48, 54, and 55 have been amended to recite "breast cancer." Support for the amendments can be found at least, for example, in claims 44 and 49 as originally filed. Claims 41 and 48 have been amended to delete unnecessary wording. Claims 43 and 48 have been amended to recite "presence or absence." Support for the amendments can be found at least, for example, at pages 7, 13, and 46. Claim 48 has been amended to recite "SEQ ID NO: 1" and "thereby to produce a complex." Support for the amendment is found in the specification at least, for example, on page 42, Table 2, and in claims 41, 43 and 48 as originally filed. Claim 45 has been amended to depend from claim 43.

Applicants submit that the amendments introduce no new matter.

The following comments address in order the remaining issues raised in the Office action.

Information Disclosure Statement

Applicants thank Examiner Harris for the invitation to supply additional copies of the documents listed in the previously filed information disclosure statements. Applicants intend to file a supplemental IDS including these documents.

Claim Objections

The Office action objects to claims 48-55 as referencing non-elected SEQ ID numbers. All claims have been amended to reference SEQ ID NO: 1. In view of this amendment, Applicants respectfully request that this objection be reconsidered and withdrawn.

Claim Rejections Under 35 U.S.C. § 112, first paragraph, written description

Claims 9-20 presently stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. Claims 9-20 have been canceled without prejudice and without acquiescing to the rejections thereto. In view of the foregoing claim cancellations, Applicants respectfully request that this rejection under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Claim Rejections Under 35 U.S.C. § 112, second paragraph

Claims 9-20, 41, 42 and 48-55 presently stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Claims 9-20 and 49 have been canceled without prejudice and without acquiescing to the rejections thereto. The remaining claims have been amended to delete the term "cancer-associated." In view of the amendments, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Claim Rejections Under 35 U.S.C. § 102(b)

Claims 9-11 and 15-17 presently stand rejected under 35 U.S.C. § 102(b), as allegedly anticipated by Adams *et al.* (1983) Cancer Res. 43(9):4297-4301. Claims 9-20 and 49 have been canceled without prejudice and without acquiescing to the rejections thereto. In view of the foregoing claim cancellations, Applicants respectfully request that this rejection under 35 U.S.C. § 102(b) be reconsidered and withdrawn.

Claim Rejections Under 35 U.S.C. § 102(e)

Claims 9-20, 41-47 and 55 presently stand rejected under 35 U.S.C. § 102(e), as allegedly anticipated by U.S. Patent Application Publication number 2002/0081659 ("Rosen"), noting that sequence 687 of Rosen comprises SEQ ID NO: 1 of the present application and that the five hundred forty-fifth paragraph of Rosen mentions breast cancer. Claims 9-20 and 44 have been cancelled thereby obviating this rejection. Applicants respectfully traverse this rejection to the extent that it is maintained over claims 41-43, 45-47 and 55 as amended, for the following reasons.

Applicants submit that it is well settled that, for a reference to anticipate a claim under 35 U.S.C. 102(e), the "reference must clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound without *any* need for picking, choosing, and combining...." In re Arkley, 455 F.2d 586, 587 (CCPA 1972) (emphasis in original). A § 102 rejection is "proper only when the claimed subject matter *is* identically disclosed or described in 'the prior art.'" Id. at 587 (emphasis in original). Furthermore, Applicants submit that it is well settled law that a "claimed invention cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled." Amgen v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1354 (Fed. Cir. 2003). See also In re Donohue, 766 F.2d 531 (Fed. Cir. 1985) (holding that a non-enabled disclosure does not constitute prior art under 35 U.S.C. § 102).

Applicants respectfully submit that Rosen does not describe that sequence number 687 is a marker for breast cancer because it fails to point to this particular combination without random "picking, choosing, and combining" from a group appearing to contain four hundred fifty-nine sequences, several hundred possible indications, and four possible uses. Furthermore, because Rosen fails to enable one skilled in the art to make or use sequence number 687 as a marker for breast cancer, it cannot anticipate the present application under 35 U.S.C. § 102(e). Each of these issues is addressed in more detail below.

I. Rosen does not describe that sequence number 687 can be used a marker for breast cancer without random "picking, choosing, and combining."

The Arkley court held that a rejection under 35 U.S.C. § 102 is only proper when "the claimed subject matter *is* identically disclosed or described in 'the prior art.'" Id. at 587 (emphasis in original). The Arkley court further held that for a "rejection under 35 U.S.C. § 102(e) to have been proper, the . . . reference must clearly and unequivocally disclose the claimed [invention] or direct those skilled in the art to the [invention] without *any* need for picking, choosing, and combining various disclosures not directly related to each other by the teachings of the cited reference." Id (emphasis in original). In reversing a claim rejection under 35 U.S.C. § 102(e), the Arkley court referred to In re Ruschig, 379 F.2d 990 (CCPA 1967), which analogized an invention to a particular tree in a forest and held an application did not describe a particular invention where the application lacked "blaze marks which single out particular trees." Ruschig at 995. In Ruschig, the applicants claimed N-(p-chlorobenzenesulfonyl)-N-propylurea, yet they only disclosed a general class of benzenesulfonylureas with two substituents, one of which can be placed in each of the three positions on the benzene ring. Id. at 991, 994. The Examiner calculated that at least 1,010 compounds were disclosed by this description. Id. at 994. The Ruschig court held, therefore, that "while [...] naming is not essential, something more than the disclosure of a class of 1000, or 100, or even 48, compounds is required." Id. The appellants argued that "guides" to N-(p-chlorobenzenesulfonyl)-N-propylurea were provided in the specification, for example, by listing one particular substituent together with 18 others. Id. at 995. The Ruschig court found this argument unpersuasive because it did not lead one to conclude that one substituent was preferred to the other 18. Id. at 995. The Ruschig court held, therefore, that N-(p-chlorobenzenesulfonyl)-N-propylurea was not adequately described in the specification and affirmed the rejection of the claimed subject matter. Id. at 995, 996.

Similarly, Rosen does not "clearly and unequivocally" describe that the protein identified by sequence number six hundred eighty-seven is a marker for breast cancer, nor does it guide one skilled in the art to it. To illustrate the analogy with Ruschig, it may be helpful to consider the

Rosen reference as describing a method with three independent substituents: a sequence, an indication, and a possible use. The "substituent" space in Rosen includes four hundred fifty-nine polypeptide sequences, an estimated several hundred indications (listed in paragraphs 425-548), and up to four possible uses for each indication: diagnosis, prognosis, prevention, and treatment. Similar to Ruschig, nowhere in Rosen is sequence number six hundred eighty-seven pointed out as associated with breast cancer and nowhere is it indicated that this sequence can be used for the diagnosis (as opposed to prognosis, prevention, or treatment) of breast cancer. "Breast cancer," for example, is listed in paragraph 545 of Rosen which also appears to contain 70 other indications. This particular paragraph alone appears to provide no fewer than 130,356 possibilities (459 sequences x 71 indications x 4 uses). Applicants estimate the total number of possible indications listed between paragraphs 425-548 of Rosen application to be several hundred. Accordingly, Rosen appears to teach at least several hundred thousand different possibilities.

Applicants submit that Rosen does not reasonably lead a person skilled in the art to any particular sequence associated with either diagnosis, prognosis, prevention, or treatment of any particular indication without random "picking, choosing, and combining." In fact, Rosen fails to provide guidance to a single combination of the elements discussed above. Applicants fail to see any "blaze marks" provided in the Rosen application that would lead anyone to reasonably believe that sequence number 687 was "preferred" as a tool for detection of breast cancer. In contrast to Rosen, the present application "clearly and unequivocally" claims sequence number 1 (SEQ ID NO: 1) as a marker for breast cancer.

Because the Rosen application does not "clearly and equivocally" describe diagnosing breast cancer in a mammal using a protein comprising SEQ ID NO: 1 as a marker, Applicants submit that the Rosen application cannot anticipate the claimed invention.

II. Rosen does not enable the use of sequence number 687 as a marker for breast cancer.

For a reference to be enabling, it is well settled that a person skilled in the art should be able to practice the invention without "undue experimentation." MPEP 2164.01. See also In re Wands, 858 F.2d 731 (Fed. Cir. 1988). The factors courts consider when determining whether experimentation is "undue" include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. MPEP 2164.01(a).

When this test is applied to Rosen, Applicants submit that Rosen clearly does not enable one skilled in the art to practice using sequence number 687 as a marker for breast cancer without "undue experimentation." Addressing factors (A) and (B), the present invention is directed to the specific use of sequences comprising SEQ ID NO: 1 as markers for breast cancer. Addressing factor (F), Rosen provides little or no direction regarding the use of sequence number 687 or any other sequence comprising the present SEQ ID NO:1 as a marker for breast cancer. As discussed above, there are at least hundreds of thousands of possible combinations of sequences, possible indications, and possible uses based on the teachings of Rosen, and that there is no teaching whatsoever leading the skilled artisan to combine sequence number 687 and breast cancer diagnosis. Addressing factor (G), there are no working examples of the use of sequence 687 as a breast cancer marker. There is not even a prophetic example that sequence 687 can be used as a breast cancer marker. Addressing factor (H), in view of the absence of specific guidance in Rosen pointing specifically to sequence 687 as a breast cancer marker, Applicants submit that the quantity of experimentation needed to practice the present invention based on the content of the Rosen disclosure is very large, as one of skill in the art would need to test each sequence disclosed in Rosen for each recited possible indication and for each recited possible use before learning which combinations were of any use. Addressing factors (C)-(E), Applicants submit that based on the level of ordinary skill in the art, the state and unpredictability of the art, and the lack of direction provided by Rosen, the usefulness of sequence 687 as a breast cancer marker

was not predictable absent the specific teachings of the present application. Applicants submit, therefore, that Rosen does not enable one skilled in the art to use sequence number 687 as a marker for breast cancer as required by Amgen and, therefore, does not qualify as prior art under 35 U.S.C. § 102(e).

In summary, Applicants respectfully submit that Rosen does not qualify as an anticipatory reference under 35 U.S.C. § 102(e) because it does not describe the invention as required by Arkley, and because it does not enable the invention as required by Amgen. Accordingly, Applicants respectfully request that the rejection of pending claims 41-43, 45-48 and 50-55 be reconsidered and withdrawn.

Claim Rejections Under 35 U.S.C. § 103

Claims 9-20 presently stand rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over Adams *et al.* (Cancer Research 43(9): 4297-4301, 1983), and further in view of Rosen. Claims 9-20 have been canceled without prejudice and without acquiescing to the rejections thereto. In view of the foregoing claim cancellations, Applicants respectfully request that this rejection be reconsidered and withdrawn.

CONCLUSION

Claims 41-43, 45-48 and 50-55 are pending and presented for consideration. The Examiner is invited to telephone the undersigned attorney to discuss any remaining issues.

Respectfully submitted,

Date: March 25, 2004
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